MONOGRAPH #34:

POLYNEUROPATHY: CLASSIFICATION BY NERVE CONDUCTION STUDIES AND ELECTROMYOGRAPHY

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Electrodiagnostic evaluation of patients with suspected polyneuropathy is useful for detecting and documenting peripheral abnormalities, identifying the predominant pathophysiology, and determining the prognosis for certain disorders. The electrodiagnostic classification of polyneuropathy is associated with morphologic correlates and is based upon determining involvement of sensory and motor fibers and distinguishing between predominantly axon loss and demyelinating lesions. Accurate electrodiagnostic classification leads to a more focused and expedient identification of the etiology of polyneuropathy in clinical situations.

Key words: polyneuropathy • electrodiagnosis • nerve conduction studies • electromyography
with nerve transection. Recovery was prolonged, occurring first in muscles closest to the site of damage, and related to regeneration of the axon via intact endoneurial tubes. "Neurapraxia" was used to define a motor paralysis not associated with axonal degeneration; recovery occurred within hours to months.

Histopathologic evaluation of experimental nerve compression has increased our understanding of "neurapraxia." Defects have been demonstrated under the edges of the compressing tourniquet without extension throughout the compressed area. Invagination of one myelin segment into the next has been associated with conduction block by occluding the node of Ranvier, resulting in ionic current blockade.

Electrodiagnostic evaluation of polyneuropathy is similar to the evaluation of focal nerve lesions. It is necessary to determine the presence of sensory and motor fiber involvement and to accurately distinguish between axon loss and demyelinating lesions. Clearly, many polyneuropathies are neither purely axonal or demyelinating, but rather a combination of both with predominance of one or the other. The results of conventional electroneuromyography usually can make this distinction.

**PHYSIOLOGIC BASIS OF ELECTRODIAGNOSTIC ABNORMALITIES**

The characteristic electrodiagnostic findings in purely axon loss lesions are best demonstrated following total axonal interruption as in nerve transection. Attention to the sequential abnormalities is useful in identifying those components of the electrodiagnostic examination most sensitive to axonal disorders. Landau demonstrated that muscle contraction could be evoked for several days with stimulation of a transected nerve; the response then diminished with complete loss of excitability after 4 to 5 days.

Clinical electrodiagnostic evaluation demonstrates similar findings. Immediately after transection, motor and sensory evoked response amplitude, conduction velocity, and distal latency remain normal with stimulation distal to the lesion. Needle electromyography demonstrates normal insertional and rest activity, although voluntary motor unit action potentials (MUAPs) cannot be activated. Within days, a progressive decrease in compound muscle action potential (CMAP) and sensory nerve action potential (SNAP) amplitude occurs. Evoked responses ultimately disappear after 3 to 7 days. Prior to disappearance, sensory and motor conduction velocities and distal latencies remain essentially normal with only minimal abnormalities at a time when amplitude is substantially diminished. Insertional and rest abnormalities on needle electromyography can be apparent within 7 to 10 days, although may not be evident for up to 3 weeks depending upon the proximity of the denervated muscle to the site of nerve section. Initial abnormality consists of prolonged insertional activity, followed by the appearance of sustained positive waves, spontaneous fibrillation potentials, and complex repetitive discharges.

With incomplete axon loss lesions, reduced recruitment is recorded rather than complete absence of voluntary MUAPs. MUAPs initially are of normal amplitude, duration, and configuration. A slight increase in the percentage of polyphasic MUAPs may appear after 10 to 14 days, presumably secondary to sprouting or collateral regeneration of surviving motor axons. Within months, MUAPs are of increased amplitude and duration with an increased percentage of polyphasic potentials.

In contrast, different electrodiagnostic results are obtained following either focal or diffuse demyelination. With a complete focal conduction block, initial findings are identical to those described for nerve transection. Motor and sensory evoked responses cannot be demonstrated with nerve stimulation proximal to the lesion; however, stimulation distal to the lesion results in normal responses. Regardless of the duration of the physiologic block, all nerve conduction studies distal to the lesion remain normal. Insertional and resting abnormalities may not develop on needle examination. If present, those abnormalities are modest, commensurate with the mild degree of axon loss often resulting from insults severe enough to produce conduction block.

The electrodiagnostic abnormalities associated with focal demyelination without conduction block are similar to those seen in chronic nerve compression, ie, substantial reduction of conduction velocity across the lesion.

In uniform demyelinating disorders, the marked reduction of conduction velocity is disproportionate to the relatively normal evoked response amplitude with distal stimulation. There is relatively homogeneous involvement of all myelinated fibers.

With multifocal demyelination, conduction velocity may also be reduced disproportionate to the relatively preserved evoked response amplitude with distal stimulation. Proximal stimulation re-
sults in abnormal temporal dispersion of the response, the proximal response being of substantially lower amplitude and longer duration than the distal response (Figure 1). Reduced conduction velocity in some fibers increases temporal dispersion by accentuating the differences in conduction of different fibers within the nerve. Partial conduction block can contribute to diminished amplitude. Distal demyelination may be associated with prolonged distal latency.

Needle electromyography demonstrates decreased recruitment (attributable to conduction block in some fibers) and MUAPs may show increased polyphasia, presumably secondary to distal demyelination. Other characteristic findings associated with denervation are not present on needle electromyography unless superimposed axon loss exists.

ELECTRODIAGNOSTIC EVALUATION IN SUSPECTED POLYNEUROPATHY

The collective results of nerve conduction studies and electromyography are useful in analyzing the underlying pathophysiology, and this data, together with the clinical findings, may suggest a specific diagnosis in addition to giving an approximation to the disease duration.

Complete electrodiagnostic examination of a polyneuropathy requires both motor and sensory conduction studies, preferably upon multiple nerves in upper and lower extremities. Bilateral studies should be performed on several peripheral nerves to demonstrate the characteristic symmetry of abnormality. Since individuals with polyneuropathy are susceptible to focal trauma, it is not unusual to find a clinical mononeuropathy superimposed upon a mild polyneuropathy. All individuals with mononeuropathy should be evaluated for an underlying polyneuropathy.

A relatively standardized electrodiagnostic evaluation (Table 1) is recommended for the evaluation of polyneuropathy, although the strategy may differ depending upon severity. In individuals with mild symptoms and signs, the electromyographer is advised to evaluate the most sensitive or susceptible peripheral nerves.

For example, in a typical diffuse polyneuropathy, motor and sensory nerve conduction studies of the distal lower extremity are more likely to be abnormal than those in the upper extremity. Similarly, needle electromyography of the intrinsic

Table 1. Polyneuropathy protocol.

<table>
<thead>
<tr>
<th>Conduction Studies</th>
<th>Needle Examination</th>
</tr>
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<tbody>
<tr>
<td>Test most involved site when mild or moderate, least involved if severe</td>
<td>Examine anterior tibial, medial gastrocnemius, first dorsal interosseous (hand), and lumbar paraspinal muscles. If normal, intrinsic foot muscles should be examined.</td>
</tr>
<tr>
<td>Peroneal motor (extensor digitorum brevis); stimulate at ankle and knee. Record F response latency following distal antidromic stimulation. If abnormal, tibial motor (abductor hallucis); stimulate at ankle and knee; record F response latency. If no responses: Peroneal motor (anterior tibial); stimulate at fibula and knee. Ulnar motor (hypothenar); stimulate at elbow and wrist. Median motor (thenar); stimulate at elbow and wrist. Measure F response latency. Sural sensory (ankle): stimulate 14 cm from recording electrode; perform conduction velocity unless amplitude supernormal. If not clearly normal because of age or technical factors, consider: Needle recording. Averaging. Median sensory (index); stimulate wrist and elbow. If antidromic response is absent or a focal entrapment is suspected, record from the wrist stimulating the palm. Additional peripheral nerves can be evaluated if findings equivocal. Definite abnormalities should result in: Evaluation of opposite extremity. Proceed to evaluation of specific suspected abnormality.</td>
<td></td>
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<tr>
<td>If prominent cranial involvement: Facial motor (orbicularis oculi); stimulate at angle of jaw. Blink reflex studies (orbicularis oculi); stimulate supraorbital nerve.</td>
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</tbody>
</table>

FIGURE 1. Ulnar motor nerve conduction study recording from the abductor digiti minimi muscle in a patient with chronic inflammatory demyelinating polyneuropathy. Marked temporal dispersion of the proximal compound motor action potential (CMAP) on elbow stimulation (B) is recorded compared with the distal CMAP on stimulation at the wrist (A).
foot muscles may demonstrate abnormality not present in upper extremity muscles. Conversely, evoked responses may be absent in the distal lower extremities in individuals with moderately severe symptoms and signs, making it impossible to determine the presence of a demyelinating component. Additional studies should be performed using proximal nerves as well as upper extremity or facial nerves.

Needle electromyography is useful in grossly defining the chronicity of an axon loss lesion, based upon the distribution and amplitude of fibrillation potentials and positive waves, as well as MUAP parameters. The distribution of needle abnormality is useful in identifying other disorders that may be confused with, or superimposed upon, an underlying polyneuropathy. For example, distal predilection of abnormality, greater in the lower than upper extremities, is characteristic of most axon loss polyneuropathies. Moderately severe, asymmetric involvement of lower extremity muscles, sparing the intrinsic foot muscles, although not completely inconsistent with a diagnosis of polyneuropathy, would be more consistent with old poliomyelitis, other motorneuron disorders, or polyradiculopathy. Similarly, marked abnormality on examination of paraspinal muscles is unusual in polyneuropathy and suggests a superimposed polyradiculopathy.

**CLASSIFICATION OF POLYNEUROPATHY BASED UPON ELECTRODIAGNOSTIC FINDINGS**

Although a universally accepted electrodiagnostic classification is improbable, a useful model can be created using the predominant electrodiagnostic abnormalities. In this classification, polyneuropathy is divided into six categories based upon the prevalence of sensory and motor as well as axon and myelin involvement. Demyelinating polyneuropathies are subdivided into uniform and segmental disorders. Discussion will be devoted to the clinical and electrodiagnostic aspects of one or two common polyneuropathies within each category; polyneuropathies with similar electrodiagnostic characteristics are listed in a table under each classification. Only polyneuropathies with documented electrophysiologic abnormalities are listed. Some etiologies are listed under more than one category as they can manifest several types of diffuse and symmetric polyneuropathy. Carcinoma, acquired immune deficiency syndrome (AIDS), and lupus erythematosus are examples of the latter.

**Table 2. Uniform demyelinating, mixed sensorimotor polyneuropathy.**

| Hereditary motor sensory neuropathy types I, III, IV | 45, 68, 71, 74, 76 |
| Metachromatic leukodystrophy | 53, 67 |
| Krabbe's globoid leukodystrophy | 100, 151 |
| Adrenomyeloneuropathy | 107, 237 |
| Congenital hypomyelinating neuropathy | 101, 102, 106 |
| Tangier disease | 53 |
| Cockayne's syndrome | 98, 189 |
| Cerebrotendinous xanthomatosis | 51, 121 |
inherited or congenital diseases with similar electrodiagnostic findings.

**Segmental Demyelinating, Motor > Sensory Polyneuropathy.** Acute inflammatory demyelinating polyneuropathy (AIDP, Guillain–Barré syndrome) is of unknown etiology, but is preceded by an infection in 70% of individuals, raising the hypothesis of an immunologic origin. This is supported by the efficacy of therapeutic plasma exchange in treating AIDP.

This disorder commonly presents with distal paresthesias followed by symmetric weakness of extremity and cranial muscles, usually sparing extraocular muscles and sphincters.\(^1\) Weakness predominates and increases for 1 to 4 weeks. Additional findings include areflexia and cytoalbuminodissociation after 1 week. An associated autonomic neuropathy may coexist. Pathologic studies verify the inflammatory and demyelinating involvement of the peripheral nerve that may be associated with severe, secondary axonal and even anterior horn cell degeneration.

Electrodiagnostic findings are variable. In 1965, Lambert and Mulder reported electrodiagnostic studies for 49 patients evaluated during the first 3 weeks of illness: 14% had no abnormality of conduction, 61% had conduction velocities less than 70% of the normal mean, and 25% demonstrated prolonged distal latencies with minimal or no slowing of conduction velocities.\(^1\) Serial evaluation of the latter group demonstrated sequential slowing of conduction velocity in some patients similar to the second group described above.

The large percentage of patients with normal conduction studies probably reflected the state of electrodiagnosis at that time when motor conduction studies were emphasized and sensory conduction studies, H reflexes, and F waves were not in general use. Variability in reported electrodiagnostic findings can be explained by understanding the temporal changes following acute axonal degeneration and by recognizing this as a multifocal rather than a diffuse disorder.

We analyzed sequential electrodiagnostic data for 70 consecutive patients with AIDP.\(^4\) During the first 5 weeks of illness, motor conduction study abnormalities (abnormal CMAP temporal dispersion and/or conduction block, reduced amplitude, slowed conventional or terminal conduction velocity, and prolonged or absent F responses) were more common than sensory conduction abnormalities. Early in the disease (weeks 1 to 2), abnormalities of motor amplitudes were much more common than slowing in distal or proximal motor conduction rates. In the case of F responses, the latency was often prolonged out of proportion to that expected when the distal motor latencies and limb conduction velocities were considered, results indicating proximal nerve involvement.

Using pooled data, the nadir of abnormality occurred during the third week for motor conduction studies and during the fourth week for sensory conduction studies. Motor study abnormalities tended to be homogeneous, while sensory study abnormalities were patchy, revealing defects of individual nerves and normalcy of other sensory nerves. Most notably, in approximately half of patients during the first 4 weeks of disease, sural studies were normal in the setting of abnormal median sensory results, findings atypical in any diffuse polyneuropathy. Normal conduction studies were unusual: only one patient manifested no abnormality of conduction during the first 5 weeks of illness. Using criterion for assessing the presence of demyelination, 87% of patients had evidence of a prominent demyelinating neuropathy in at least one nerve not localizable to a common entrapment site. Two patients were classified as having axonal degeneration only; indeterminate results were recorded in 10% of patients.

On needle electromyography, abnormal spontaneous activity appeared between weeks 2 and 4, while abnormalities of MUAP morphology (increased polyphasia and amplitude) became apparent during weeks 4 to 5. No patient had normal MUAP recruitment at the time of initial examination.

Chronic inflammatory demyelinating polyneuropathy (CIDP) is a disorder of presumed immunologic etiology, presenting as a slowly progressive, stepwise progressive, or monophasic illness in the majority of patients.\(^7\) A relapsing and remitting course is seen in approximately one-third of patients.\(^23\) Weakness involves cranial, truncal, and extremity musculature. Pathologically, there is evidence for mononuclear cell infiltration, segmental demyelination, and hypertrophic changes most often observed in spinal roots, spinal ganglia, and proximal nerve trunks. Electrodiagnostic findings in the individual patient are indistinguishable from AIDP. On occasion, sensory evoked responses are spared. Motor conduction velocity may improve concurrent with clinical remission, but disproportionally less than the degree of clinical improvement would suggest. Nevertheless, a poor correlation exists between slowing of
motor nerve conduction velocity and the severity of muscle weakness, and conduction velocity often remains severely reduced during clinical remission. Needle examination usually demonstrates distal greater than proximal limb and paraspinal muscle denervation.

Several types of polyneuropathy are associated with plasma cell dyscrasias. One type, a severe chronic demyelinating polyneuropathy, has been associated with osteosclerotic myeloma, Waldenstrom's macroglobulinemia, and monoclonal gammopathy of undetermined significance. Clinical and electrodiagnostic features are similar to those of CIDP.

On a global scale, leprosy is the most common cause of peripheral neuropathy. It is best conceived as a mononeuropathy of superficial sensory nerve branches within cutaneous lesions, with subsequent involvement of major motor branches. A symmetric sensory and motor distal polyneuropathy should never be found, although involvement may be so widespread as to suggest a diffuse process. The neuropathy of leprosy is classified under this category because the clinical presentation of multiple mononeuropathies and the pathologic and electrodiagnostic features of segmental demyelination most mimic a motor greater than sensory demyelinating polyneuropathy. Slowed conduction velocity and/or proximal conduction block of motor nerves across focal areas of involvement is common. Adjacent motor nerves may be normal.

Other diseases manifesting electrodiagnostically as segmental demyelinating, motor greater than sensory polyneuropathy are listed in Table 3. Multifocal demyelinating polyneuropathy with persistent conduction block is of particular interest to the electromyographer because this potentially treatable neuropathy clinically resembles motorneuron disease.

### Table 3. Segmental demyelinating, motor > sensory polyneuropathy.

<table>
<thead>
<tr>
<th>Condition</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute inflammatory demyelinating polyneuropathy</td>
<td>4, 12, 141</td>
</tr>
<tr>
<td>Chronic inflammatory demyelinating polyneuropathy</td>
<td>57, 73, 203</td>
</tr>
<tr>
<td>Multifocal demyelinating polyneuropathy with persistent conduction block</td>
<td>30, 149, 195, 197, 212</td>
</tr>
<tr>
<td>Osteosclerotic myeloma</td>
<td>23, 124, 125, 126</td>
</tr>
<tr>
<td>Waldenstrom's macroglobulinemia</td>
<td>23, 124</td>
</tr>
<tr>
<td>Monoclonal gammopathy of undetermined significance</td>
<td>58, 106, 123, 124, 225</td>
</tr>
<tr>
<td>Gamma heavy chain disease</td>
<td>123, 124, 126</td>
</tr>
<tr>
<td>Angiolytic lymph node hyperplasia</td>
<td>108, 123, 124, 251</td>
</tr>
<tr>
<td>Hypothyroidism</td>
<td>136</td>
</tr>
<tr>
<td>Leprosy</td>
<td>40, 164, 210, 213</td>
</tr>
<tr>
<td>Diphtheria</td>
<td>136</td>
</tr>
<tr>
<td>Acute arsenic polyneuropathy</td>
<td>67</td>
</tr>
<tr>
<td>Pharmaceuticals</td>
<td>Amiodarone</td>
</tr>
<tr>
<td>Perhexilene</td>
<td>54, 144</td>
</tr>
<tr>
<td>High dose Ara-C</td>
<td>26</td>
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<tr>
<td>Lymphoma</td>
<td>13</td>
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<tr>
<td>Carcinoma</td>
<td>56</td>
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<tr>
<td>AIDS</td>
<td>14, 47, 62, 167, 193, 206</td>
</tr>
<tr>
<td>Lyme disease</td>
<td>226</td>
</tr>
<tr>
<td>Acromegaly</td>
<td>95</td>
</tr>
<tr>
<td>Hereditary neuropathy with susceptibility to pressure palsies</td>
<td>20, 165, 261</td>
</tr>
<tr>
<td>Systemic lupus erythematosus</td>
<td>68</td>
</tr>
<tr>
<td>Glue snifing neuropathy</td>
<td>128</td>
</tr>
<tr>
<td>Post porocaval anastomosis</td>
<td>236</td>
</tr>
<tr>
<td>Neuropathy associated with progressive external ophthalmoplegia</td>
<td>90, 169, 190</td>
</tr>
<tr>
<td>Ulcerative colitis</td>
<td>56</td>
</tr>
<tr>
<td>Marinesco–Sjogren syndrome</td>
<td>5</td>
</tr>
<tr>
<td>Cryoglobulinemia</td>
<td>53</td>
</tr>
</tbody>
</table>

### Axon Loss, Motor > Sensory Polyneuropathy.

Acute intermittent porphyria is an autosomal dominant disorder with incomplete penetrance, presentings as a classic triad of psychosis, abdominal pain, and polyneuropathy clinically resembling AIDP. Pathology of peripheral nerve reveals axonal degeneration with secondary demyelination. Nerve conduction studies demonstrate reduced motor evoked amplitudes, whereas conduction velocity slowing is spared until substantial reduction of amplitude occurs. Sensory evoked amplitudes are reduced in approximately 50% of patients. Fibrillation potentials appear in paraspinal muscles in 7 to 10 days and subsequently appear in other proximal and then distal muscles symmetrically.

Similar electrodiagnostic findings to porphyria may be observed in lead polyneuropathy, although there may be greater involvement of upper than lower extremities.

Hereditary motor sensory neuropathy type II (neuronal Charcot–Marie–Tooth disease) is a dominantly inherited sensorimotor polyneuropathy with insidious onset in the third to fourth decade; associated features include moderate to severe atrophy, pes cavus, hammer toes, and mild sensory loss. Motor evoked amplitudes are reduced with essentially normal conduction velocities. Sensory responses are absent in 50% of patients. Needle electromyography demonstrates chronic neurogenic changes, most prominent distally.

Although most pharmaceutically induced polyneuropathies present as a sensory greater than motor axonopathy, several medications produce, as an adverse effect, motor greater than sensory...
involvement. Dapsone neuronopathy is an example of such involvement.2,100,239

Table 4 lists other polyneuropathies with electrodiagnostic features similar to porphyria and HMSN type II.

**Sensory Axon Loss Neuronopathy.** Carcinomatous sensory neuronopathy is the most distinctive of the remote-effect polyneuropathies associated with carcinoma. Its onset is subacute, often preceding identification of the neoplasm by several months. A strong association exists between oat cell carcinoma of the lung and a sensory neuronopathy. Symptoms and signs include pain, paresthesias, dyesthesias, and large, more than small, fiber sensory loss.111 Areflexia, gait ataxia, and choreoathetoid movements are common, but strength is usually preserved.111 Neuropathology reveals inflammation and cell loss in dorsal root ganglia, and gliosis of the posterior column of the spinal cord. Nerve conduction studies usually reveal diminished or absent SNAP amplitudes in the setting of normal motor nerve conduction studies.111 Motor amplitudes and conduction may be slightly reduced in severe cases, perhaps representing disuse atrophy, axonal stenosis, or a combination of both. Needle examination is usually normal except in late, severe disease when spontaneous activity at rest may be recorded.

Friedreich's ataxia is a recessively inherited disorder characterized by ataxia, mild weakness, areflexia, and dissociated sensory loss involving modalities classically interpreted as reflecting posterior column dysfunction (abnormal vibration, two-point discrimination, and joint position sensation). Associated signs include scoliosis, pescavus deformity, extensor plantar responses, nystagmus, and optic atrophy. Sensory responses are usually absent, although responses of markedly reduced amplitude may be recorded.36,163,200 Motor evoked responses may be of borderline-low amplitude with slightly reduced conduction velocity.74 Moderate slowing of motor conduction velocity is occasionally reported and may be related to selective loss of large myelinated fibers.200 Mild, chronic neurogenic changes on needle electromyography may be evident, most prominently in the distal lower extremities.

Table 5 lists other diseases with the highly characteristic and unique electrodiagnostic findings recorded in sensory neuronopathy.

**Axon Loss, Mixed Sensorimotor Polyneuropathy.** The majority of toxic and metabolic polyneuropathies manifest evidence of degeneration of the distal portion of the axon. In general, these polyneuropathies are electrodiagnostically indistinguishable from one another. Sensory symptoms and signs may initially predominate, and sensory evoked amplitudes may be reduced early in the course of the disease, when motor studies are normal. Conduction velocity is normal until there is a substantial reduction of amplitude, although predilection for large fibers may reduce the maximum conduction velocity slightly. Distal latency may be slightly prolonged, prior to reduction of evoked amplitude, perhaps in association with distal axonostenosis. In contradistinction to primary demyelinating disorders, appreciable temporal dispersion of the proximal, compared with distal, CMAP is not recorded (Figure 2). Fibrillation potentials and positive waves may be seen symmetri-
FIGURE 2. Peroneal motor nerve conduction study recording from the extensor digitorum brevis muscle in a patient with a chronic sensorimotor axonal polyneuropathy. The amplitude, shape, and duration of the compound motor action potential recorded on ankle stimulation (A) does not appreciably change on stimulation at the fibular head (B).

cally in distal extremity muscles. These abnormalities on needle examination typically precede clinical evidence of motor involvement.

A common example is the polyneuropathy associated with chronic alcoholism and secondary nutritional deficiency. The clinical features are those of a symmetric and generalized sensorimotor distal polyneuropathy. Patients complain of paresthesias and dysesthesias of the feet and distal legs, more so than weakness. Physical findings consist of absent or diminished sensation in a distal to proximal gradient in the lower extremities, absent ankle reflexes, and mild weakness of toe and ankle extension. Involvement of the proximal lower extremity and hands only occurs in severe, progressive alcoholic polyneuropathy.

A detailed list of disorders associated with an axonal sensorimotor polyneuropathy and presenting with similar electrodiagnostic findings is found in Table 6.

Mixed Axon Loss and Demyelinating Sensorimotor Polyneuropathy. Diabetic polyneuropathy is the most common polyneuropathy in North America. It also represents a polyneuropathy demonstrating evidence of both axonal degeneration and demyelination. Even though several classifications of diabetic neuropathy exist, this monograph will discuss only the commonly observed, diffuse, symmetric sensorimotor polyneuropathy.

Patients characteristically manifest paresthesias, disabling dysesthesias, or numbness in the distal lower extremities. Examination demonstrates reduced vibratory sensation and two-point discrimination in a distal-to-proximal gradient in the lower extremities; proprioception may also be impaired in severe cases. This apparent dissociative sensory loss relates to predilection of large fiber involvement. In more severe disease, small fi-

Table 6. Axon loss, mixed sensorimotor polyneuropathy.

| Amyloidosis | 32, 126, 127 |
| Chronic liver disease | 119, 131 |
| Nutritional diseases |  |
| Vitamin B12 deficiency | 81, 162, 161 |
| Foliate deficiency | 29, 80 |
| Whipple’s disease | 50 |
| Post-gastrectomy syndrome | 15 |
| Gastric restriction surgery for obesity | 1 |
| Thiamine deficiency | 180 |
| Alcoholism | 9, 220, 233 |
| Sarcoidosis | 80, 182, 187 |
| Connective tissue diseases |  |
| Rheumatoid arthritis | 96, 174, 199 |
| Parietofrontal nodosa | 59 |
| Systemic lupus erythematosus |  |
| Churg-Strauss vasculitis | 59, 126 |
| Temporal arteritis | 37 |
| Scleroderma | 76 |
| Bechet’s disease | 178 |
| Hypereosinophilia syndrome | 171, 243 |
| Cryoglobulinemia | 160 |
| Toxic neuropathy | 215 |
| Acrylamide | 86, 147 |
| Carbon disulfide | 18, 226 |
| Dichlorophenoxyacetic acid | 89 |
| Ethylene oxide | 62, 97, 197 |
| Hexacarbons | 7, 142 |
| Carbon monoxide | 227 |
| Organophosphorus esters | 61 |
| Glue sniffing | 8, 134, 147 |
| Metal neuropathy |  |
| Chronic arsenic intoxication | 42 |
| Mercury | 3 |
| Thallium | 16, 60 |
| Gold | 130, 241 |
| Pharmaceuticals |  |
| Colchicine | 156 |
| Phenytoin | 507, 230 |
| Ethambutol | 176 |
| Amitriptyline | 150 |
| Metronidazole | 31, 69 |
| Misonidazole | 96 |
| Nitrofurantoin | 81, 229 |
| Chloroquine | 7 |
| Disulfiram | 10, 21, 37, 295 |
| Glutathione | 184 |
| Nitrous Oxide | 107, 145, 216 |
| Lithium | 16, 162 |
| Carcinomatous axonal sensorimotor polyneuropathy | 51 |
| Chronic obstructive pulmonary disease | 76, 173 |
| Giant axonal dystrophy | 13, 129, 132, 204, 232 |
| Olivopontocerebellar atrophy | 44, 211 |
| Neuropathy of chronic illness | 24, 29, 252 |
| Acromegaly | 115 |
| Hypophosphatemia |  |
| Lymphomatous axonal sensorimotor polyneuropathy | 242 |
| Hypothyroidism | 65, 156, 179, 201 |
| Myotonic dystrophy | 52, 54, 165, 172 |
| Necrotizing angiopathy | 70, 130, 218 |
| Lyme disease | 129, 233 |
| AIDS, ARC | 25, 62, 152, 167, 193 |
| Jamaican neuropathy | 37, 217 |
| Tangier disease | 152, 202 |
| Gouty neuropathy | 83 |
| Polycythemia vera | 250 |
| Typical multiple myeloma | 126 |
lers are involved as evidenced by alteration of pain and temperature sensation and dysautononia. The major pathologic abnormalities are segmental demyelination and remyelination, in addition to axonal degeneration.231

The electrodiagnostic findings in distal symmetric diabetic polyneuropathy are variable, especially in early or mild cases. In most patients, sensory conduction studies reveal diminished evoked amplitude with moderate slowing of conduction velocity, greater than expected from axonal degeneration alone. Concurrently or later in the course of disease, motor evoked responses demonstrate similar findings with the addition of temporally dispersed proximal responses.224 Occasionally, in patients with asymptomatic or mild polyneuropathy, slowing in motor conduction velocity will be the only electrodiagnostic abnormality.246 Fibrillation potentials may appear in intrinsic foot muscles symmetrically prior to clinical evidence of atrophy or weakness, or reduced CMAP amplitudes recorded from foot muscles.

Polyneuropathy is relatively common in chronic renal failure, and virtually all patients requiring dialysis have evidence of a distal sensorimotor polyneuropathy. In many patients, this manifests as an axon loss, mixed sensorimotor polyneuropathy with borderline low motor and sensory evoked amplitudes.28 In other patients, nerve conduction studies demonstrate pronounced slowing in conduction velocity with preserved proximal CMAPs. These latter findings reflect the mixed components of segmental demyelination superimposed upon axon loss, verified pathologically by Dyck and colleagues.72 Fibrillation potentials are seen in distal extremity muscles, particularly the intrinsic foot muscles. Unfortunately, determination of motor nerve conduction velocities alone is probably the most widely accepted measurement of peripheral nerve function in the evaluation of and serial assessment of uremic polyneuropathy. While widely accepted as a measure of adequacy of dialysis, conduction velocity determinations alone are likely inadequate and unreliable unless changes are marked.133

For completeness, Table 7 lists the two polyneuropathies manifesting electrophysiologically as a mixed axon loss and demyelinating sensorimotor polyneuropathy.

**SOURCES OF ERROR**

The primary sources of error in evaluation of patients with suspected polyneuropathy are errors of omission, i.e., drawing conclusions based upon a limited database. Another common error is overemphasizing the value of "conduction velocity." This measure is sensitive to demyelination but may remain normal in the setting of axonal degeneration. Similarly, distal latencies, another barometer of conduction rate, are markedly prolonged only in demyelination, moderately prolonged in association with axonal scarring, and only mildly prolonged in axonal degeneration.

Another pitfall is the failure to exclude from interpretation focal slowing of conduction velocity due to specific entrapment mononeuropathies before concluding that a generalized process of reduced conduction exists. Particularly vulnerable to entrapment are the ulnar and peroneal nerves at the elbow and knee, respectively, and the median nerve at the wrist.

Motor and sensory evoked amplitudes are extremely sensitive to axonal degeneration despite the wide range of normal values. Markedly reduced motor evoked amplitudes with normal sensory responses are unusual in polyneuropathy; further investigation usually demonstrates a polyradiculopathy, motorneuron disease, or defective neuromuscular transmission (generalized low motor-normal sensory syndrome).245

Sensitivity of conduction velocity, distal latency, and evoked response amplitude to change in temperature requires careful measurement and maintenance of proper limb temperature (32°C to 36°C, surface temperature). Warming a limb by 5°C may result in as much as a 10-m/s increase in conduction velocity, a 1-ms decrease in distal latency, and a 20% decrease in sensory and motor amplitude.

Needle electromyography of intrinsic foot muscles is a sensitive measure of potential axonal degeneration. Nevertheless, these muscles may also be subject to local trauma and false-positive studies. This situation is most commonly observed in the extensor digitorum brevis and abductor digiti minimi muscles, while the abductor hallucis and first dorsal interosseous muscles are less likely to give aberrant results.89 Careful sampling of individual muscles and documentation of bilaterality

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**Table 7.** Mixed axon loss, demyelinating sensorimotor polyneuropathy.

<table>
<thead>
<tr>
<th>Diabetes Mellitus</th>
<th>892, 142, 158, 224, 231, 246</th>
</tr>
</thead>
<tbody>
<tr>
<td>Uremia</td>
<td>20, 43, 72, 133</td>
</tr>
</tbody>
</table>

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reduces the likelihood of false positive findings secondary to local injury.

In summary, a carefully planned and performed electrodiagnostic study is useful in quantifying and defining the underlying pathophysiology in polyneuropathy. In addition, interpretation of the results of electrodiagnosis often suggests a specific diagnosis, particularly when combined with other laboratory and clinical information.

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